Jiang 09/869,540

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=> d his 1

     (FILE 'MEDLINE, HCAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT
     16:17:06 ON 25 JUN 2003)
L34          32 DUP REM L33 (32 DUPLICATES REMOVED)

=> d que l34
L1           32 SEA FILE=REGISTRY MLRCMLGRVYRPCWQV/SQSP
L2           55 SEA L1
L3        20492 SEA MORI M?/AU
L10       45845 SEA (L3 OR L4 OR L5 OR L6 OR L7 OR L8 OR L9)
L11          31 SEA L10 AND MELANIN#(5A) HORMONE#
L12          24 SEA L11 AND (SLC? OR SLT?)
L15          13 SEA L2 AND (SLC? OR SLT?)
L16          35 SEA L12 OR L15
L17        3027 SEA MELANIN#(5A) HORMONE#
L18        8981 SEA SLC?
L19        4007 SEA SLT?
L20         206 SEA L17 AND (L18 OR L19)
L21         166 SEA SOMATOSTATIN(3A) LIKE(3A) RECEPTOR?
L22          11 SEA L17 AND L21
L23         207 SEA L20 OR L22
L24          27 SEA L23 AND (BIND?(5A)(ASSAY? OR MEASUR? OR DETECT? OR
                SCREEN?))
L25           6 SEA L23 AND (BIND?(5A)(PROPERT? OR CAPA?))
L26           6 SEA L23 AND (BIND?(5A)(INCREASE? OR DECREASE? OR REDUC? OR
                ALTER? OR CHANG?))
L27          62 SEA L16 OR (L24 OR L25 OR L26)
L28           2 SEA FILE=REGISTRY "BOLTON-HUNTER REAGENT"/CN
L29         197 SEA L28
L30        2967 SEA BOLTON(A) HUNTER
L31           2 SEA (L29 OR L30) AND MELANIN#(5A) HORMONE#
L32           2 SEA (L29 OR L30) AND (SLC? OR SLT? OR SOMATOSTATIN(3A)
                LIKE(3A) RECEPTOR?)
L33          64 SEA L27 OR L31 OR L32
L34          32 DUP REM L33 (32 DUPLICATES REMOVED)


=> d ibib abs l34 1-32

L34  ANSWER 1 OF 32  HCAPLUS  COPYRIGHT 2003 ACS       DUPLICATE 1
ACCESSION NUMBER:        2003:389258  HCAPLUS
TITLE:                   Orphan GPCR ligands related to obesity
AUTHOR(S):               Fujisawa, Yukio; Mori, Masaaki; Ohtaki,
                         Tetsuya; Hinuma, Shuji; Fujino, Masahiko
CORPORATE SOURCE:        Discovery Research Laboratories I, Ibaraki, 300-4293,
                         Japan
SOURCE:                  Current Medicinal Chemistry: Central Nervous System
                         Agents (2003), 3(2), 101-120
                         CODEN: CMCCCO; ISSN: 1568-0150
PUBLISHER:               Bentham Science Publishers Ltd.
DOCUMENT TYPE:           Journal
LANGUAGE:                English
AB   In this article, we describe recent advances in the study of novel orphan
     GPCR ligands related to obesity, focusing on melanin-concg.
     hormone (MCH), neuropeptide W (NPW), neuropeptide B (NPB) and
     galanin-like peptide (GALP). An endogenous ligand of orphan
     G-protein-coupled receptor (GPCR), SLC-1 (MCH-R1), was isolated
     from rat brain and revealed to be MCH. Phenotypic analyses of genetically
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engineered animals indicated that the MCH-**SLC**-1/MCH-R1 axis is relevant to feeding behavior and energy homeostasis. We developed MCH receptor antagonists and found that they could inhibit food intake stimulated by central administration of MCH. NPW was isolated from porcine hypothalamus as a ligand for orphan GPR8 and found to bind to both GPR7 and GPR8 at similar EDs. Results of intracerebroventricular administration of NPW to rats suggested that it regulated feeding behavior and the neuroendocrine system, although further study is required to confirm the physiol. functions of NPW. In addn., we isolated NPB, which was closely related to NPW in structure, from bovine hypothalamus as a GPR7 ligand and found that it was modified with bromine at position C-6 of the indole ring of the N-terminal Trp residue. From the distribution of the NPB mRNA in the rat brain, NPB was suggested to be involved in the regulation of feeding and the neuroendocrine system as well as memory and learning. GALP was isolated from porcine small intestines as a ligand for galanin subtype receptor GALR2. The most interesting feature was that GALP-neurons were specifically localized to the arcuate nucleus in rats and under the pos. regulation of leptin, suggesting that GALP mediates the anorexic activity of leptin.

REFERENCE COUNT: 109 THERE ARE 109 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 2 OF 32 MEDLINE DUPLICATE 2
ACCESSION NUMBER: 2003163264 IN-PROCESS
DOCUMENT NUMBER: 22567054 PubMed ID: 12680590
TITLE: Different structural requirements for **melanin**-concentrating **hormone** (MCH) interacting with rat MCH-R1 (**SLC**-1) and mouse B16 cell MCH-R.
AUTHOR: Schlumberger Sophie E; Saito Yumiko; Giller Thomas; Hintermann Edith; Tanner Heidi; Jaggin Verena; Zumsteg Urs; Civelli Olivier; Eberle Alex N
CORPORATE SOURCE: Laboratory of Endocrinology, Department of Research (ZLF), University Hospital and University Children's Hospital, Basel, Switzerland.
SOURCE: JOURNAL OF RECEPTOR AND SIGNAL TRANSDUCTION RESEARCH, (2003 Feb) 23 (1) 69-81.
Journal code: 9509432. ISSN: 1079-9893.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: IN-PROCESS; NONINDEXED; Priority Journals
ENTRY DATE: Entered STN: 20030409
Last Updated on STN: 20030409

AB **Melanin**-concentrating **hormone** (MCH) is a neuropeptide occurring in all vertebrates and some invertebrates and is now known to stimulate pigment aggregation in teleost melanophores and food-intake in mammals. Whereas the two MCH receptor subtypes hitherto cloned, MCH-R1 and MCH-R2, are thought to mediate mainly the central effects of MCH, the MCH-R on pigment cells has not yet been identified, although in some studies MCH-R1 was reported to be expressed by human melanocytes and melanoma cells. Here we present data of a structure-activity study in which 12 MCH peptides were tested on rat MCH-R1 and mouse B16 melanoma cell MCH-R, by comparing receptor binding affinities and biological activities. For receptor binding analysis with HEK-293 cells expressing rat MCH-R1 (**SLC**-1), the radioligand was [125I]-[Tyr13]-MCH with the natural sequence. For B16 cells (F1 and G4F sublines) expressing B16 MCH-R, the analog [125I]-[D-Phe13, Tyr19]-MCH served as radioligand. The bioassay used for MCH-R1 was intracellular Ca2+ mobilization quantified

with the FLIPR instrument, whereas for B16 MCH-R the signal determined was MAP kinase activation. Our data show that some of the peptides displayed a similar relative increase or decrease of potency in both cell types tested. For example, linear MCH with Ser residues at positions 7 and 16 was almost inactive whereas a slight increase in side-chain hydrophilicity at residues 4 and 8, or truncation of MCH at the N-terminus by two residues hardly **changed binding** affinity or bioactivity. On the other hand, salmonic MCH which also lacks the first two residues of the mammalian sequence but in addition has different residues at positions 4, 5, 9, and 18 exhibited a 5- to 10-fold lower binding activity than MCH in both cell systems. A striking difference in ligand recognition between MCH-R1 and B16 MCH-R was however observed with modifications at position 13 of MCH: whereas L-Phe13 in [Phe13, Tyr19]-MCH was well tolerated by both MCH-R1 and B16 MCH-R, change of configuration to D-Phe13 in [D-Phe13, Tyr19]-MCH or [D-Phe13]-MCH led to a complete loss of biological activity and to a 5- to 10-fold lower binding activity with MCH-R1. By contrast, the D-Phe13 residue increased the affinity of [D-Phe13, Tyr19]-MCH to B16 MCH-R about 10-fold and elicited MAP kinase activation as observed with [Phe13, Tyr19]-MCH or MCH. These data demonstrate that ligand recognition by B16 MCH-R differs from that of MCH-R1 in several respects, indicating that the B16 MCH-R represents an MCH-R subtype different from MCH-R1.

L34 ANSWER 3 OF 32 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:31754 HCAPLUS
DOCUMENT NUMBER: 136:79781
TITLE: Method for screening MCH receptor antagonist/agonist
INVENTOR(S): **Mori, Masaaki**; **Shimomura, Yukio**; Harada, Mioko; **Sugo, Tsukasa**; Shintani, Yasushi
PATENT ASSIGNEE(S): Takeda Chemical Industries, Ltd., Japan
SOURCE: PCT Int. Appl., 112 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002003070	A1	20020110	WO 2001-JP5809	20010704
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 2001069440	A5	20020114	AU 2001-69440	20010704
EP 1298439	A1	20030402	EP 2001-947822	20010704
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				

PRIORITY APPLN. INFO.: JP 2000-208254 A 20000705
WO 2001-JP5809 W 20010704

AB A method for screening compds. or salts thereof which change the affinity of MCH or a salt thereof with **SLT** or a salt thereof, or its peptide fragment or its amide or its ester or its salt, characterized in

that it comprises using MCH or a deriv. thereof or its salt, and **SLT** or a salt thereof or its peptide fragment or its amide or its ester or its salt. The method is useful as a method for screening **SLT** agonists which can be used as an appetite stimulating agent and the like, and **SLT** antagonists which can be used as a preventive/ therapeutic agent for obesity and the like.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 4 OF 32 SCISEARCH COPYRIGHT 2003 THOMSON ISI
ACCESSION NUMBER: 2002:360599 SCISEARCH
THE GENUINE ARTICLE: 543HR
TITLE: Synthesis and biological evaluation in vitro of a selective, high potency peptide agonist of human **melanin**-concentrating **hormone** action at human **melanin**-concentrating **hormone** receptor 1
AUTHOR: Bednarek M A (Reprint); Tan C; Hreniuk D L; Palyha O C; MacNeill D J; Van der Ploeg L H Y; Howard A D; Feighner S D
CORPORATE SOURCE: Merck Res Labs, Dept Med Chem, R50G-141, Rahway, NJ 07065 USA (Reprint); Merck Res Labs, Dept Med Chem, Rahway, NJ 07065 USA; Merck Res Labs, Dept Obes & Metab Disorders, Rahway, NJ 07065 USA
COUNTRY OF AUTHOR: USA
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (19 APR 2002) Vol. 277, No. 16, pp. 13821-13826.
Publisher: AMER SOC BIOCHEMISTRY MOLECULAR BIOLOGY INC, 9650 ROCKVILLE PIKE, BETHESDA, MD 20814-3996 USA.
ISSN: 0021-9258.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 30

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Human **melanin**-concentrating **hormone** (hMCH) is a nonselective natural ligand for the human **melanin**-concentrating **hormone** receptors: hMCH-1R and hMCH-2R. Similarly, the smaller peptide encompassing the disulfide ring and Arg(6) of hMCH, Ac-Arg(6)-cyclo(S-S)(Cys(7)-Met(8)-Leu(9)-Gly(10)-Arg(11)-Val(12)-Tyr(13)-Arg(14)-Pro(15)-Cys(16)).-NH2, Ac-hMCH(6-16)-NH2, binds to and activates equally well both human MCH receptors present in the brain. To separate the physiological functions of hMCH-1R from those of hMCH-2R, new potent and hMCH-1R selective agonists are necessary. In the present study, analogs of Ac-hMCH(6-16)-NH2 were prepared and tested in **binding** and functional **assays** on cells expressing the MCH receptors. In these peptides, Arg in position 6 was replaced with various D-amino acids and/or Gly in position 10 was substituted with various L-amino acids. Several of the new compounds turned out to be potent agonists at hMCH-1R with improved selectivity over hMCH-2R. For example, peptide 26 with D-Arg in place of L-Arg in position 6 and Asn in place of Gly in position 10, Ac-DArg(6)-cyclo(S-S)(Cys(7)-Met(8)-Leu(9)-Asn(10)-Arg(11)-Val(12)-Tyr(13)-Arg(14)-Pro(15)-Cys(16))-NH2, was a potent hMCH-1R agonist (IC50 = 0.5 nM, EC50 = 47 nM) with more than 200-fold selectivity with respect to hMCH-2R. Apparently, these structural changes in positions 6 and 10 results in peptide conformations that allow for efficient interactions with hMCH-1R but are unfavorable for molecular recognition at hMCH-2R.

L34 ANSWER 5 OF 32 SCISEARCH COPYRIGHT 2003 THOMSON ISI
ACCESSION NUMBER: 2002:432005 SCISEARCH

Search completed by David Schreiber 308-4292

Jiang 09/869,540

THE GENUINE ARTICLE: 552ZX
TITLE: Synthesis and biological evaluation in vitro of selective, high affinity peptide antagonists of human **melanin**-concentrating **hormone** action at human **melanin**-concentrating **hormone** receptor 1
AUTHOR: Bednarek M A (Reprint); Hreniuk D L; Tan C; Palyha O C; MacNeil D J; Van der Ploeg L H Y; Howard A D; Feighner S D
CORPORATE SOURCE: Merck Res Labs, Dept Med Chem, R50G-141, Rahway, NJ 07065 USA (Reprint); Merck Res Labs, Dept Med Chem, Rahway, NJ 07065 USA; Merck Res Labs, Dept Obes & Metab Disorders, Rahway, NJ 07065 USA
COUNTRY OF AUTHOR: USA
SOURCE: BIOCHEMISTRY, (21 MAY 2002) Vol. 41, No. 20, pp. 6383-6390

Publisher: AMER CHEMICAL SOC, 1155 16TH ST, NW, WASHINGTON, DC 20036 USA.
ISSN: 0006-2960.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 33

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Human **melanin**-concentrating **hormone** (hMCH) and many of its analogues are potent but nonspecific ligands for human **melanin**-concentrating **hormone** receptors 1 and 2 (hMCH-1R and hMCH-2R). To differentiate between the physiological functions of these receptors, selective antagonists are needed. In this study, analogues of Ac-Arg(6)-cyclo(S-S)(Cys(7)-Met(8)-Leu(9)-Gly(10)-Arg(11)-Val(12)-Tyr(13)-Arg(14)-Pro(15)-Cys(16))-NH2, a high affinity but nonselective agonist at hMCH-1R and hMCH-2R, were prepared and tested in **binding**, and functional **assays** on cells expressing these receptors. In the new analogues, 5-aminovaleric acid (Ava) was incorporated in place of the Leu(9)-Gly(10) and/or Arg(14)-Pro(15) segments of the disulfide ring. Several of these compounds turned out to be high affinity antagonists selective for hMCH-1R. Moreover, even at micromolar concentrations, they were devoid of agonist potency at both hMCH receptors and not effective as hMCH-2R antagonists. For example, peptide 14, Gva(6)- cyclo(S-S)(Cys(7)-Met(8)-Leu(9)-Gly(10)-Arg(11)-Val(12)-Tyr(13)-Ava(14,15)-Cys(16))-NH2, (Gva = 5-guanidinovaleric acid), was a full competitive hMCH-1R antagonist (IC50 = 14 nM, K-B = 0.9 nM) with more than 1000-fold selectivity over hMCH-2R. Examination of various compounds with Ava in positions 9,10 and/or 14,15 revealed that the Leu(9)-Gly(10) and Arg(14)-Pro(15) segments of the disulfide ring are the principal structural elements determining hMCH-1R selectivity and ability to act as a hMCH-1R antagonist.

L34 ANSWER 6 OF 32 MEDLINE DUPLICATE 3
ACCESSION NUMBER: 2002382468 MEDLINE
DOCUMENT NUMBER: 22126156 PubMed ID: 12130742
TITLE: Appetite-boosting property of pro-**melanin**-concentrating **hormone**(131-165) (neuropeptide-glutamic acid-isoleucine) is associated with proteolytic resistance.
AUTHOR: Maulon-Feraille Laurence; Della Zuana Odile; Suply Thomas; Rovere-Jovene Carole; Audinot Valerie; Levens Nigel; Boutin Jean A; Duhault Jacques; Nahon Jean-Louis
CORPORATE SOURCE: Institut de Pharmacologie Moleculaire et Cellulaire-Centre National de la Recherche Scientifique, Unite Mixte de Recherche 6097, 660 route des Lucioles-Sophia-Antipolis, 06560 Valbonne, France.

Search completed by David Schreiber 308-4292

SOURCE: JOURNAL OF PHARMACOLOGY AND EXPERIMENTAL THERAPEUTICS, (2002 Aug) 302 (2) 766-73.
Journal code: 0376362. ISSN: 0022-3565.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200208
ENTRY DATE: Entered STN: 20020720
Last Updated on STN: 20020830
Entered Medline: 20020829

AB **Melanin**-concentrating **hormone** (MCH) is a cyclic neuropeptide, with a major role in stimulation of feeding behavior in mammals. MCH signals in the brain occur via two seven-transmembrane G protein-coupled receptors, namely MCH1 (**SLC**-1, MCH(1), MCH-R1, or MCH-1R) and MCH2 (**SLT**, MCH(2), MCH-R2, or MCH-2R). In this study, we demonstrate that the pro-MCH(131-165) peptide neuropeptide-glutamic acid-isoleucine (NEI)-MCH is more potent than MCH in stimulating feeding in the rat. Using rat MCH1-expressed human embryonic kidney 293 cells, we show that NEI-MCH exhibits 5-fold less affinity in a **binding assay** and 2-fold less potency in a cAMP assay than MCH. A similar 7- to 8-fold shift in potency was observed in a Ca(2+)(i) assay using rat MCH1 or human MCH2-transfected Chinese hamster ovary cell models. This demonstrates that NEI-MCH is not a better agonist than MCH at either of the MCH receptors. Then, we compared the proteolysis resistance of MCH and NEI-MCH to rat brain membrane homogenates and purified proteases. Kinetics of peptide degradation using brain extracts indicated a t(1/2) of 34.8 min for MCH and 78.5 min for NEI-MCH with a specific pattern of cleavage of MCH but not NEI-MCH by exo- and endo-proteases. Furthermore, MCH was found highly susceptible to degradation by aminopeptidase M and endopeptidase 24.11, whereas NEI-MCH was fully resistant to proteolysis by these enzymes. Therefore, our results strongly suggest that reduced susceptibility to proteases of NEI-MCH compared with MCH account for its enhanced activity in feeding behavior. NEI-MCH represents therefore the first MCH natural functional "superagonist" so far described.

L34 ANSWER 7 OF 32 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2002:424385 HCAPLUS
DOCUMENT NUMBER: 138:32614
TITLE: **Melanin**-concentrating **hormone** receptor antagonist as antiobesity agent
AUTHOR(S): **Mori, Masaaki; Suzuki, Nobuhiro;** Fujino, Masahiko
CORPORATE SOURCE: Research Department of Medicinal Drugs, Takeda Chemical Industries Ltd., Japan
SOURCE: Molecular Medicine (Tokyo, Japan) (2002), 39(4), 448-454
CODEN: MOLMEL; ISSN: 0918-6557
PUBLISHER: Nakayama Shoten
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Japanese
AB A review. It has been identified that **melanin**-concg. **hormone** (MCH) as the natural ligand for the orphan somatostatin-like receptor 1 (**SLC**-1). A role for MCH in the central regulation of feeding behavior in transgenic mice and a novel selective MCH receptor antagonist T-226296 as a antiobesity agent is reviewed.

Search completed by David Schreiber 308-4292

L34 ANSWER 8 OF 32 MEDLINE DUPLICATE 4
ACCESSION NUMBER: 2002177014 MEDLINE
DOCUMENT NUMBER: 21906700 PubMed ID: 11909603
TITLE: T-226296: a novel, orally active and selective **melanin**-concentrating **hormone** receptor antagonist.
AUTHOR: **Takekawa Shiro**; Asami Asano; Ishihara Yuji; Terauchi Jun; Kato Kaneyoshi; **Shimomura Yukio**; **Mori Masaaki**; Murakoshi Hitomi; Kato Koki; **Suzuki Nobuhiro**; Nishimura Osamu; Fujino Masahiko
CORPORATE SOURCE: Discovery Research Laboratories I, Pharmaceutical Research Division, Takeda Chemical Industries, Ltd., Wadai 10, Ibaraki 300-4293, Tsukuba, Japan.
SOURCE: EUROPEAN JOURNAL OF PHARMACOLOGY, (2002 Mar 8) 438 (3) 129-35.
Journal code: 1254354. ISSN: 0014-2999.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200206
ENTRY DATE: Entered STN: 20020324
Last Updated on STN: 20020627
Entered Medline: 20020626

AB Through the screening of our in-house chemical compound library, we found a novel **melanin**-concentrating **hormone** (MCH) receptor antagonist, T-226296, a (-) enantiomer of N-[6-(dimethylamino)-methyl]-5,6,7,8-tetrahydro-2-naphthalenyl]-4'-fluoro[1,1'-biphenyl]-4-carboxamide. T-226296 exhibited high affinity for cloned human and rat MCH receptors (**SLC**-1) in receptor **binding assays** (IC50=5.5+/-0.12 nM for human **SLC**-1; 8.6+/-0.32 nM for rat **SLC**-1). T-226296 had high selectivity over other receptors, including the second subtype of the MCH receptor, **SLT** (MCH2), transporters and ion channels. In Chinese hamster ovary (CHO) cells expressing human **SLC**-1, T-226296 reversed the MCH-mediated inhibition of forskolin-stimulated cAMP accumulation, inhibited MCH-induced intracellular Ca2+ increase, and also inhibited MCH-stimulated arachidonic acid release. In rats, oral administration of T-226296 (30 mg/kg) almost completely suppressed the food intake induced by intracerebroventricular injection of MCH. These results clearly indicate that T-226296 is a novel, orally active and selective MCH receptor antagonist that will be promising for further exploring the physiology and pathophysiology of MCH-**SLC**-1 signaling.

L34 ANSWER 9 OF 32 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:816453 HCAPLUS
DOCUMENT NUMBER: 135:357943
TITLE: Preparation of 2-(aminomethyl or heterocyclylmethyl)-6-aminoquinoline and -naphthalene derivatives as **melanin** concentrating **hormone** antagonists
INVENTOR(S): Ishihara, Yuji; **Suzuki, Nobuhiro**; **Takekawa, Shiro**
PATENT ASSIGNEE(S): Takeda Chemical Industries, Ltd., Japan
SOURCE: PCT Int. Appl., 223 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1

Search completed by David Schreiber 308-4292

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001082925	A1	20011108	WO 2001-JP3614	20010426
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 2001052596	A5	20011112	AU 2001-52596	20010426
EP 1285651	A1	20030226	EP 2001-925947	20010426
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2002241274	A2	20020828	JP 2001-132357	20010427

PRIORITY APPLN. INFO.: JP 2000-134295 A 20000428
JP 2000-384897 A 20001213
WO 2001-JP3614 W 20010426

OTHER SOURCE(S): MARPAT 135:357943

AB **Melanin** concg. **hormone** (MCH) antagonists contg. compds. of the general formula Ar1-X-Ar-Y-NR1R2 or salts thereof (wherein Ar1 is an optionally substituted cyclic group; X and Y are each independently a spacer having a C1-6 main chain; Ar is an optionally substituted fused polycyclic arom. ring; R1 and R2 are each independently hydrogen or an optionally substituted hydrocarbon group, or alternatively R1 and R2 together with the nitrogen atom adjacent thereto may form a nitrogenous heterocycle, or R2 together with the nitrogen atom adjacent thereto and Y may form an optionally substituted nitrogenous heterocycle, or R2 together with the nitrogen atom adjacent thereto, Y, and Ar may form a fused ring) are described. They are appetite depressants and useful as preventive or therapeutic drugs for diseases caused by **melanin** concg. **hormone**, in particular obesity. Thus, tert-Bu 6-(N,N-dimethylaminomethyl)-2-naphthylcarbamate (prepn. given) was treated with CF3CO2H and condensed with 4'-chloro-1,1'-biphenyl-4-carboxylic acid using 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride in the presence of 4-dimethylaminopyridine in DMF at room temp. for 16 h to give 4'-chloro-N-[6-(N,N-dimethylaminomethyl)-2-naphthyl]-1,1'-biphenyl-4-carboxamide (I). I in vitro inhibited the binding of [35S]-guanosine 5'-(.gamma.-thio)triphosphate to CHO cell line expressing the MCH receptor, i.e. the orphan G protein-coupled receptor **SLC**-1, with IC50 of 5 nM. A tablet formulation contg. I was described.

REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 10 OF 32 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:713558 HCAPLUS
DOCUMENT NUMBER: 135:268320
TITLE: **Melanin**-concentrating **hormone** receptor GPRv17 cDNA from human and monkey and medical uses
INVENTOR(S): Kurama, Takeshi; Matsumoto, Shunichiro; Takasaki, Jun; Matsumoto, Mitsuyuki; Kamohara, Masazumi; Saito, Tetsu; Oda, Tamaki; Saito, Youko
PATENT ASSIGNEE(S): Yamanouchi Pharmaceutical Co., Ltd., Japan; Helix Research Institute

SOURCE: PCT Int. Appl., 62 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001070975	A1	20010927	WO 2001-JP2343	20010323

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: JP 2000-88588 A 20000324

AB CDNAs encoding a novel **melanin**-concg. **hormone** (MCH) receptor GPRv17 from human and monkey, recombinant expression, use in screening antagonists as drug candidates for prevention and therapy for obesity and eating disorder, and reagent for detecting the gene, are disclosed. **Changes** in GTP **binding** activity, [Ca2+]i, or [cAMP] can be used for screening. A DNA fragment encoding an amino acid sequence possessing common features to the G protein-coupled receptor (GPCR) superfamily was found in the human genomic sequence, and from this information, the full-length cDNA of a novel GPCR, designated GPRv17, was cloned from the human fetal brain cDNA library. GPRv17 showed the highest homol. to the **melanin**-concg. **hormone** (MCH) receptor, **SLC**-1 (38% identity). Recombinant expression in 293 cells, confirmation of specific **binding** to MCH and **screening** of antagonists, are described. Strong expression in the brain, esp. in hypothalamus, cerebral cortex, hippocampus, amygdala, and nucleus (substantia) nigra, was detected. Prepn. of antibodies is also described.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 11 OF 32 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:636105 HCAPLUS
DOCUMENT NUMBER: 135:206479
TITLE: Human G protein-coupled receptors and uses in treatment of mental disorder
INVENTOR(S): Vogeli, Gabriel; Wood, Linda S.; Parodi, Luis A.; Lind, Peter
PATENT ASSIGNEE(S): Pharmacia + Upjohn Company, USA
SOURCE: PCT Int. Appl., 279 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001062797	A2	20010830	WO 2001-US5676	20010223
WO 2001062797	A3	20021024		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,

CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR,
HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT,
LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,
SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN,
YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

EP 1265925	A2	20021218	EP 2001-912924	20010223
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
US 2003003451	A1	20030102	US 2001-791932	20010223

PRIORITY APPLN. INFO.:

US 2000-184247P	P	20000223
US 2000-184303P	P	20000223
US 2000-184304P	P	20000223
US 2000-184305P	P	20000223
US 2000-184397P	P	20000223
US 2000-186457P	P	20000302
US 2000-186810P	P	20000303
US 2000-188064P	P	20000309
US 2000-188880P	P	20000313
US 2000-194344P	P	20000403
US 2000-213861P	P	20000623
US 2000-217369P	P	20000711
US 2000-217370P	P	20000711
US 2000-218337P	P	20000714
US 2000-218492P	P	20000720
US 2000-219492P	P	20000720
WO 2001-US5676	W	20010223

AB The present invention provides cDNA encoding sixty human G protein-coupled receptor polypeptides. In addn., the invention provides expression vectors, host cells and methods for prodn. of human G protein-coupled receptor polypeptides. The invention provides tissue expression profile for cDNA encoding human G protein-coupled receptors. The invention also provides methods for the identification of G protein-coupled receptor modulators, useful for the treatment of human diseases and conditions. The invention further provides methods and kit to diagnose mental disorder or genetic susceptibility related to human G protein-coupled receptors. The invention also provides antibody for human G protein-coupled receptors.

L34 ANSWER 12 OF 32 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:228703 HCAPLUS
DOCUMENT NUMBER: 134:252267
TITLE: Preparation of diarylalakanediamine derivatives as **melanin** concentrating **hormone** (MCH) antagonists
INVENTOR(S): Kato, Kaneyoshi; **Mori, Masaaki; Suzuki, Nobuhiro; Shimomura, Yukio; Takekawa, Shiro**; Choh, Nobuo
PATENT ASSIGNEE(S): Takeda Chemical Industries, Ltd., Japan
SOURCE: PCT Int. Appl., 284 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

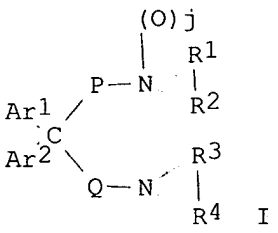
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 2001021169	A1	20010329	WO 2000-JP6376	20000919	
W:	AE, AG, AL, AM, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CN, CR, CU, CZ, DM, DZ, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MA, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TM, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 2000073158	A5	20010424	AU 2000-73158	20000919	
JP 2002097138	A2	20020402	JP 2000-288894	20000919	
EP 1219294	A1	20020703	EP 2000-961076	20000919	
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				

PRIORITY APPLN. INFO.: JP 1999-266278 A 19990920
JP 2000-221055 A 20000717
WO 2000-JP6376 W 20000919

OTHER SOURCE(S): MARPAT 134:252267

GI



I

AB Compds. of general formula [I; wherein Ar1 and Ar2 are each an optionally substituted arom. group; P and Q are each a divalent aliph. hydrocarbon group which may contain ethereal oxygen or sulfur in the carbon chain and may be substituted; R1 and R3 are each (i) hydrogen, (ii) acyl, or (iii) optionally substituted hydrocarbyl; R2 and R4 are each (i) hydrogen, (ii) optionally substituted alkyl, or (iii) optionally substituted alkylcarbonyl; alternatively R1 and R2 or R3 and R4 together with the nitrogen atom adjacent thereto may form a monocyclic or fused nitrogenous heterocyclic group; and j is 0 or 1], salts of the same, or prodrugs thereof are prepd. These compds. are useful for the treatment of diseases caused by MCH, e.g. obesity (as antiobesity agents) or overeating (as appetite depressants), or for the improvement of emotional disorders or sexual function. Thus, benzyl 2-[(5-hydroxy-2,2-diphenylpentyl)amino]-2-oxoethylcarbamate was brominated by Br and Ph3P in MeCN at room temp. for 1 h to give benzyl 2-[(5-bromo-2,2-diphenylpentyl)amino]-2-oxoethylcarbamate which was dissolved in MeCN, treated with 4-phenylpiperidine and K2CO3 in MeCN, and stirred at 40.degree. overnight to give, after purifn. on alumina column chromatog. and conversion into the HCl, benzyl 2-[[2,2-diphenyl-5-(4-phenylpiperidino)pentyl]amino]-2-oxoethylcarbamate hydrochloride (II). II in vitro inhibited the binding of [35S]-guanosine 5'-(.gamma.-thio)triphosphate to human somatostatin-like receptor (**SLC**-1) with IC50 of 5 nM. Tablet formulations contg. II were described. .

REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 13 OF 32 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:78525 HCAPLUS
DOCUMENT NUMBER: 134:126850
TITLE: Protein and cDNA sequences of human G protein-coupled receptor AXOR21, and uses thereof in therapy, diagnosis, and drug screening
INVENTOR(S): Duckworth, David Malcolm; Hill, Jeffrey; Muir, Alison Isobel; Szekeres, Philip Graham
PATENT ASSIGNEE(S): SmithKline Beecham PLC, UK
SOURCE: PCT Int. Appl., 42 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001007606	A1	20010201	WO 2000-GB2899	20000727
W: JP				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 1196572	A1	20020417	EP 2000-948173	20000727
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

PRIORITY APPLN. INFO.: GB 1999-17627 A 19990727
GB 1999-20046 A 19990824
WO 2000-GB2899 W 20000727

AB Also disclosed is . This invention provides protein and cDNA sequences for a newly identified human protein, designated AXOR21, which is believed to be a G-protein coupled receptor since it shows homol. with rat somatostatin receptor-like (**SLC1**). In one embodiment, the invention relates to drug screening assays of using AXOR21 protein and an AXOR21 ligand, melanin concg. hormone (MCH), in identifying compds. that may be agonists or antagonists that are potentially useful in therapy. Also disclosed are methods for utilizing AXOR21 polypeptides and polynucleotides in the diagnosis and treatment of diseases assocd. with inappropriate AXOR21 activity or levels.

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 14 OF 32 MEDLINE DUPLICATE 5
ACCESSION NUMBER: 2001500347 MEDLINE
DOCUMENT NUMBER: 21433976 PubMed ID: 11459838
TITLE: Identification and pharmacological characterization of a novel human **melanin**-concentrating **hormone** receptor, mch-r2.
AUTHOR: Wang S; Behan J; O'Neill K; Weig B; Fried S; Laz T; Bayne M; Gustafson E; Hawes B E
CORPORATE SOURCE: Departments of Human Genomics and Central Nervous System Biology, Schering-Plough Research Institute, Kenilworth, New Jersey 07033, USA.
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (2001 Sep 14) 276 (37) 34664-70.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

Search completed by David Schreiber 308-4292

LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AF399937
ENTRY MONTH: 200110
ENTRY DATE: Entered STN: 20010911
Last Updated on STN: 20030105
Entered Medline: 20011011

AB **Melanin**-concentrating **hormone** (MCH) is a neuropeptide highly expressed in the brain that regulates several physiological functions mediated by receptors in the G protein-coupled receptor family. Recently an orphan receptor, **SLC**-1, has been identified as an MCH receptor (MCH-R1). Herein we identify and characterize a novel receptor for human MCH (MCH-R2). The receptor is composed of 340 amino acids encoded by a 1023-base pair cDNA and is 35% homologous to **SLC**-1. (125)I-MCH specifically bound to Chinese hamster ovary cells stably expressing MCH-R2. MCH stimulated dose-dependent increases in intracellular free Ca(2+) and inositol phosphate production in these cells but did not affect cAMP production. The pharmacological profile for mammalian MCH, [Phe(13),Tyr(19)]MCH, and salmon MCH at MCH-R2 differed compared with MCH-R1 as assessed by intracellular signaling and radioligand **binding assays**. The EC(50) in signaling assays and the IC(50) in radioligand **binding assays** of salmon MCH was an order of magnitude higher than mammalian MCH at MCH-R2. By comparison, the EC(50) and IC(50) values of salmon MCH and mammalian MCH at MCH-R1 were relatively similar. Blot hybridization revealed exclusive expression of MCH-R2 mRNA in several distinct brain regions, particularly in the cortical area, suggesting the involvement of MCH-R2 in the central regulation of MCH-mediated functions.

L34 ANSWER 15 OF 32 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2001:396614 BIOSIS
DOCUMENT NUMBER: PREV200100396614
TITLE: Molecular cloning and functional characterization of MCH2, a novel human MCH receptor.
AUTHOR(S): Hill, Jeffrey (1); Duckworth, Malcolm; Murdock, Paul; Rennie, Gillian; Sabido-David, Cibele; Ames, Robert S.; Szekeres, Philip; Wilson, Shelagh; Bergsma, Derk J.; Gloger, Israel S.; Levy, Dana S.; Chambers, Jon K.; Muir, Alison I.
CORPORATE SOURCE: (1) Department of Molecular Biology, GlaxoSmithKline, New Frontiers Science Park, Third Avenue, Harlow, Essex, CM19 5AW: Jeffrey_2_Hill@gsk.com UK
SOURCE: Journal of Biological Chemistry, (June 8, 2001) Vol. 276, No. 23, pp. 20125-20129. print.
ISSN: 0021-9258.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English

AB **Melanin**-concentrating **hormone** (MCH) is involved in the regulation of feeding and energy homeostasis. Recently, a 353-amino acid splice variant form of the human orphan receptor **SLC**-1 (hereafter referred to as MCH1) was identified as an MCH receptor. This report describes the cloning and functional characterization of a novel second human MCH receptor, which we designate MCH2, initially identified in a genomic survey sequence as being homologous to MCH1 receptors. Using this sequence, a full-length cDNA was generated with an open reading frame of 1023 base pairs, encoding a polypeptide of 340 amino acids, with 38% identity to MCH1 and with many of the structural features conserved in G protein-coupled receptors. This newly discovered receptor belongs to class

1 (rhodopsin-like) of the G protein-coupled receptor superfamily. HEK293 cells transfected with MCH2 receptors responded to nanomolar concentrations of MCH with an increase in intracellular Ca2+ levels and increased cellular extrusion of protons. In addition, fluorescently labeled MCH bound with nanomolar affinity to these cells. The tissue localization of MCH2 receptor mRNA, as determined by quantitative reverse transcription-polymerase chain reaction, was similar to that of MCH1 in that both receptors are expressed predominantly in the brain. The discovery of a novel MCH receptor represents a new potential drug target and will allow the further elucidation of MCH-mediated responses.

L34 ANSWER 16 OF 32 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:329752 HCAPLUS
DOCUMENT NUMBER: 135:117301
TITLE: Structure-activity relationship studies of melanin-concentrating hormone (MCH)-related peptide ligands at **SLC**-1, the human MCH receptor
AUTHOR(S): Audinot, Valerie; Beauverger, Philippe; Lahaye, Chantal; Suply, Thomas; Rodriguez, Marianne; Ouvry, Christine; Lamamy, Veronique; Imbert, Jerome; Rique, Herve; Nahon, Jean-Louis; Galizzi, Jean-Pierre; Canet, Emmanuel; Levens, Nigel; Fauchere, Jean-Luc; Boutin, Jean A.
CORPORATE SOURCE: Division de Pharmacologie Moleculaire et Cellulaire, Institut de Recherches SERVIER, Croissy sur Seine, 78290, Fr.
SOURCE: Journal of Biological Chemistry (2001), 276(17), 13554-13562
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Melanin-concg. hormone (MCH) is a cyclic nonadecapeptide involved in the regulation of feeding behavior, which acts through a G protein-coupled receptor (**SLC**-1) inhibiting adenyl cyclase activity. In this study, 57 analogs of MCH were investigated on the recently cloned human MCH receptor stably expressed in HEK293 cells, on both the inhibition of forskolin-stimulated cAMP prodn. and guanosine-5'-O-3-[35S]thiotriphosphate ([35S]GTP.gamma.S) binding. The dodecapeptide MCH-(6-17) (MCH ring between Cys7 and Cys16, with a single extra amino acid at the N terminus (Arg6) and at the C terminus (Trp17)) was found to be the minimal sequence required for a full and potent agonistic response on cAMP formation and [35S]GTP.gamma.S binding. We Ala-scanned this dodecapeptide and found that only 3 of 8 amino acids of the ring, namely Met8, Arg11, and Tyr13, were essential to elicit full and potent responses in both tests. Deletions inside the ring led either to inactivity or to poor antagonists with potencies in the micromolar range. Cys7 and Cys16 were substituted by Asp and Lys or one of their analogs, in an attempt to replace the disulfide bridge by an amide bond. However, those modifications were deleterious for agonistic activity. In [35S]GTP.gamma.S binding, these compds. behaved as weak antagonists (KB 1-4 .mu.M). Finally, substitution in MCH-(6-17) of 6 out of 12 amino acids by non-natural residues and concomitant replacement of the disulfide bond by an amide bond led to three compds. with potent antagonistic properties (KB = 0.1-0.2 .mu.M). Exploitation of these structure-activity relationships should open the way to the design of short and stable MCH peptide antagonists.
REFERENCE COUNT: 57 THERE ARE 57 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 17 OF 32 MEDLINE DUPLICATE 6
ACCESSION NUMBER: 2001264063 MEDLINE
DOCUMENT NUMBER: 21255282 PubMed ID: 11355873
TITLE: Cloning of a novel G protein-coupled receptor, **SLT**, a subtype of the **melanin**-concentrating **hormone** receptor.
AUTHOR: **Mori M**; Harada M; Terao Y; **Sugo T**; Watanabe T; **Shimomura Y**; Abe M; Shintani Y; Onda H; Nishimura O; Fujino M
CORPORATE SOURCE: Discovery Research Laboratories I, Pharmaceutical Research Division, Takeda Chemical Industries, Ltd., Wadai 10, Tsukuba, Ibaraki, 300-4293, Japan.. Mori_Masaaski@takeda.co.jp
SOURCE: BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, (2001 May 25) 283 (5) 1013-8.
Journal code: 0372516. ISSN: 0006-291X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AB060151
ENTRY MONTH: 200106
ENTRY DATE: Entered STN: 20010702
Last Updated on STN: 20010702
Entered Medline: 20010628

AB A DNA fragment encoding an amino acid sequence possessing common features to the G protein-coupled receptor (GPCR) superfamily was found in the human genomic sequence, and from this information, the full-length cDNA of a novel GPCR, designated **SLT**, was cloned from the human hippocampus cDNA library. **SLT** showed the highest homology to the **melanin**-concentrating **hormone** (MCH) receptor, **SLC**-1 (31.5% identity), and to a lesser extent, to the somatostatin (SST) receptor subtypes. MCH exhibited agonistic behavior when applied to the **SLT**-expressing CHO cells at subnanomolar doses whereas more than 200 known peptides, including SST and cortistatin, did not. These results indicated that MCH is the cognate ligand of the **SLT** receptor and that this newly cloned GPCR is the second subtype of the MCH receptor. Quantitative polymerase chain reaction analysis of the **SLT** gene expression in human tissues showed that the **SLT** receptor is expressed mainly in brain areas including the cerebral cortex, amygdala, hippocampus, and corpus callosum, as well as in a limited number of peripheral tissues. The distribution of the **SLT** nearly overlapped that of **SLC**-1, suggesting that some of the neural functions of MCH may be mediated by both of these receptor subtypes.

L34 ANSWER 18 OF 32 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2001:575418 BIOSIS
DOCUMENT NUMBER: PREV200100575418
TITLE: **SLC**-1 receptor mediates the effect of **melanin** concentrating **hormone** on feeding behaviour in the rat: A structure activity study.
AUTHOR(S): Suply, T. (1); Della-Zuana, O. (1); Audinot, V. (1); Rodriguez, M. (1); Beauverger, P. (1); Duhault, J. (1); Canet, E. (1); Galizzi, J. P. (1); Lebrun, C. (1); Nahon, J. L.; Levens, N. (1); Boutin, J. A. (1)

Search completed by David Schreiber 308-4292

CORPORATE SOURCE: (1) Inst. de Recherches Servier, Croissy-sur-Seine France
SOURCE: Society for Neuroscience Abstracts, (2001) Vol. 27, No. 1, pp. 851. print.
Meeting Info.: 31st Annual Meeting of the Society for Neuroscience San Diego, California, USA November 10-15, 2001
ISSN: 0190-5295.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Several studies have shown that **melanin** concentrating **hormone** (MCH) is an orexigenic peptide in rat. In the present study, a structure activity relationship with MCH analogues was performed in rat, both in vitro and in vivo. On rat recombinant **SLC**-1 receptor, both cAMP inhibition and (125I)-S36057 **binding** were **measured**. In vivo, these analogues were injected intra-cerebro-ventricularly in rats and their effects were evaluated upon food intake. First, data obtained with the rat recombinant receptor were highly correlated with those obtained from its human counterpart. Second, agonist potencies in the cAMP **assay** were also highly correlated with **binding** affinities. These peptides could be classified into several groups according to their potency at the **SLC**-1 receptor (from sub-nanomolar activity to complete inactivity). Indeed, there was a strong correlation between their effects upon food intake and the results obtained at the rat **SLC**-1 receptor. The present report describes for the first time the rat **SLC**-1 receptor pharmacology and clearly establishes the relevance of the **SLC**-1 receptor in feeding behaviour.

L34 ANSWER 19 OF 32 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:723784 HCAPLUS
DOCUMENT NUMBER: 136:112829
TITLE: Cloning and molecular characterization of the novel human melanin-concentrating hormone receptor MCH2
AUTHOR(S): Rodriguez, M.; Beauverger, P.; Naime, I.; Rique, H.; Ouvry, C.; Souchaud, S.; Dromaint, S.; Nagel, N.; Suply, T.; Audinot, V.; Boutin, J. A.; Galizzi, J. P.
CORPORATE SOURCE: Institut de Recherches Servier, Division de Pharmacologie Moleculaire et Cellulaire, Croissy sur Seine, Fr.
SOURCE: Molecular Pharmacology (2001), 60(4), 632-639
CODEN: MOPMA3; ISSN: 0026-895X
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Using a genomics-based approach for screening orphan G-protein-coupled receptors, the authors have identified and cloned a novel high-affinity, melanin-concg. hormone (MCH) receptor. This receptor, named S643b, displays the greatest overall identity (32%) with the previously reported human **SLC**-1 receptor (MCH1) and to a lesser extent with the somatostatin receptor subtypes. The gene encoding the S643b receptor spans more than 23 kilobase pairs (kb) and was mapped, by radiation hybrid expts., on chromosome 6q14.3-q15. Comparison of the S643b cDNA with human genomic sequence reveals that the 340-amino-acid receptor is encoded by five exons. Its tissue distribution, as detd. by Northern blot and reverse transcription-polymerase chain reaction anal., indicates that a 4-kb transcript is predominantly expressed in the brain. When expressed in Chinese hamster ovary (CHO) cells, the S643b receptor displays a

strong, dose-dependent, transient elevation of intracellular calcium in response to MCH (EC50 = 9.5 nM). During the present study, the authors isolated a splice variant, designated S643a, encoding for a receptor that was not activated by MCH in a cellular calcium mobilization assay. Comparative pharmacol. studies using CHO cells stably expressing either **SLC**-1 or S643b receptors demonstrated that similar structural features of MCH are required to stimulate intracellular Ca2+ mobilization at both receptors. The identification and localization of this new MCH receptor (MCH2) provides further insight into the physiol. implication of MCH in modulating behavioral responses, including food intake.

REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 20 OF 32 SCISEARCH COPYRIGHT 2003 THOMSON ISI
ACCESSION NUMBER: 2001:462414 SCISEARCH
THE GENUINE ARTICLE: 437WR
TITLE: [I-125]-S36057: a new and highly potent radioligand for the **melanin**-concentrating **hormone** receptor
AUTHOR: Audinot V; Lahaye C; Suply T; Beauverger P; Rodriguez M; Galizzi J P; Fauchere J L; Boutin J A (Reprint)
CORPORATE SOURCE: Inst Rech Servier, Div Pharmacol Mol & Cellulaire, 125 Chemin de Ronde, F-78290 Croissy Sur Seine, France (Reprint); Inst Rech Servier, Div Pharmacol Mol & Cellulaire, F-78290 Croissy Sur Seine, France; Inst Rech Servier, Div Peptides & Chim Combinatoire, F-92150 Suresnes, France
COUNTRY OF AUTHOR: France
SOURCE: BRITISH JOURNAL OF PHARMACOLOGY, (JUN 2001) Vol. 133, No. 3, pp. 371-378.
Publisher: NATURE PUBLISHING GROUP, HOUNDMILLS, BASINGSTOKE RG21 6XS, HAMPSHIRE, ENGLAND.
ISSN: 0007-1188.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 26

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB 1 Shortened, more stable and weakly hydrophobic analogues of **melanin**-concentrating **hormone** (MCH) were searched as candidates for radioiodination. Starting from the dodecapeptide MCH6 (17), we found that: (1) substitution of Tyr(13) by a Phe residue; (3) addition of a 3-iodo-Tyr residue at the N-terminus; and (3) addition of a hydrophilic spacer 8-amino-3.6-dioxyoctanoyl between the 3-iodo-Tyr and MCH, 17 (compound S36057), led to an agonist more potent than MCH itself in stimulating [S-35]-GTP gammaS binding at membranes from HEK293 cells stably expressing the human MCH receptor.

2 Specific binding of [I-125]-S36057 was found in HEK293 and CHO cell lines stably expressing the human MCH receptor. This radioligand recognized a similar number of binding sites (c cr. 800 fmol mg(-1)) than [I-125]-[3-iodo Tyr(13)]-MCH.

3 However, the KI, for [(12)5T]-S36057 obtained from saturation studies (0.037 nhl) or from binding kinetics (0.046 nhl) was at least 10 fold higher to that of [I-125]-[3-iodo Tyr(13)]-MCH (0.46 nhl).

4 Affinities determined for a series of MCH analogues were similar with both radioligands, S36057 being the most potent compound tested (K-1 = 0.053 nM).

5 Finally, [I-125]-S36057 also potently labelled the MCH receptor in membranes from whole rat brain (K-D 0.044 nh 1. B-max= 11 fmolmg(-1)).

6 Tn conclusion, [I-125]-S36057 is a more potent and more stable

radioligand than [I-125]-[3-iodo Tyr(13)]-MCH that will represent a reliable tool for **binding assays** in the search of novel MCH ligands. It should also provide great help for autoradiographic studies of the MCH receptor distribution in the central nervous system.

L34 ANSWER 21 OF 32 MEDLINE DUPLICATE 7
ACCESSION NUMBER: 2001513247 MEDLINE
DOCUMENT NUMBER: 21445263 PubMed ID: 11561073
TITLE: **SLC**-1 receptor mediates effect of **melanin** -concentrating **hormone** on feeding behavior in rat: a structure-activity study.
AUTHOR: Suply T; Della Zuana O; Audinot V; Rodriguez M; Beauverger P; Duhault J; Canet E; Galizzi J P; Nahon J L; Levens N; Boutin J A
CORPORATE SOURCE: Division de Pharmacologie Moleculaire et Cellulaire, Institut de Recherches Servier, Croissy/Seine, France.
SOURCE: JOURNAL OF PHARMACOLOGY AND EXPERIMENTAL THERAPEUTICS, (2001 Oct) 299 (1) 137-46.
Journal code: 0376362. ISSN: 0022-3565.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200110
ENTRY DATE: Entered STN: 20010919
Last Updated on STN: 20011022
Entered Medline: 20011018

AB Several studies have shown that **melanin**-concentrating **hormone** (MCH) is an orexigenic peptide in rat. In the present study, a structure-activity relationship with MCH analogs was performed in rat, both in vitro and in vivo. On rat recombinant **SLC**-1 receptor, both cAMP inhibition and [(125)I]S36057 **binding** were **measured**. In vivo, these analogs were injected intracerebroventricularly in rats and their effects were evaluated upon food intake. First, data obtained with the rat recombinant receptor were highly correlated with those obtained from its human counterpart. Second, agonist potencies in the cAMP **assay** were also highly correlated with **binding** affinities. These peptides could be classified into several groups according to their potency at the **SLC**-1 receptor (from subnanomolar activity to complete inactivity). Indeed, there was a strong correlation between their effects upon food intake and the results obtained at the rat **SLC**-1 receptor. The present report describes for the first time the rat **SLC**-1 receptor pharmacology and clearly establishes the relevance of the **SLC**-1 receptor in feeding behavior.

L34 ANSWER 22 OF 32 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:824518 HCAPLUS
DOCUMENT NUMBER: 133:359245
TITLE: Assays for agonists, antagonists and inverse agonists of **melanin** concentrating **hormone** (MCH) binding to the **somatostatin-like receptor** (**SLC**-1)
INVENTOR(S): Ahmad, Sultan; Cao, Jack; Grazzini, Eric; Lembo, Paola; Walker, Philippe
PATENT ASSIGNEE(S): AstraZeneca AB, Swed.
SOURCE: PCT Int. Appl., 17 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent

Search completed by David Schreiber 308-4292

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000070347	A1	20001123	WO 2000-SE1010	20000519

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

EP 1183539	A1	20020306	EP 2000-937431	20000519

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO

PRIORITY APPLN. INFO.:
US 1999-134844P P 19990519
US 1999-138675P P 19990614
WO 2000-SE1010 W 20000519

AB Assays are provided that can be used to screen for compds. that act as agonists or antagonists of **melanin** concg. **hormone** (MCH). The **assays** are based upon the **binding** of MCH to the **SLC**-1 receptor. Compds. identified as effective modulators have potential use for the treatment of obesity and eating disorders.

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 23 OF 32 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:475797 HCAPLUS
DOCUMENT NUMBER: 133:100060
TITLE: Rat **Melanin**-Concentrating **Hormone** and derivatives as **SLC**-1 Receptor Ligand and drug screening
INVENTOR(S): **Mori, Masaaki; Shimomura, Yukio; Takekawa, Shiro; Sugo, Tsukasa; Ishibashi, Yoshihiro; Kitada, Chieko ; Suzuki, Nobuhiro**
PATENT ASSIGNEE(S): Takeda Chemical Industries, Ltd., Japan
SOURCE: PCT Int. Appl., 123 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000040725	A1	20000713	WO 1999-JP7336	19991227

W: AE, AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CR, CU, CZ, DM, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MA, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF,

CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

CA 2356412	AA	20000713	CA 1999-2356412	19991227
JP 2001141728	A2	20010525	JP 1999-371313	19991227
EP 1143000	A1	20011010	EP 1999-961418	19991227

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO

PRIORITY APPLN. INFO.:	JP 1998-374454	A	19981228
	JP 1999-122688	A	19990428
	JP 1999-249300	A	19990902
	WO 1999-JP7336	W	19991227

AB A method and reagent kits for screening a compd. or its salt **capable** of **altering** the **binding properties** of MCH or its salt to **SLC**-1 or its salt, characterized by using MCH or its deriv. or its salt and **SLC**-1 or its salt, is disclosed. Drugs contg. the compd., in particular the antiobesity drugs, are also claimed. MCH or its fragment derivatized with **Bolton-Hunter** reagent, is also claimed. **Melanin**-concg. **hormone** (MCH), which is an orexigenic peptide, was isolated and identified as the endogenous ligand of the **SLC**-1 receptor. We established a CHO cell line expressing the rat **SLC**-1 receptor to search for its endogenous ligand. The ext. of rat whole brain showed inhibition of intracellular forskolin-induced cAMP accumulation in rat **SLC**-1-expressing CHO cells and was purified. Using HPLC purifn., we isolated and identified MCH as the endogenous ligand of the **SLC**-1 receptor. The authentic MCH demonstrated a dose-dependent inhibitory effect on cAMP accumulation in forskolin-stimulated rat and human **SLC**-1-expressing CHO cells with an EC50 value of 0.2 nM for both the rat and human **SLC**-1 receptors.

REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 24 OF 32 MEDLINE DUPLICATE 8

ACCESSION NUMBER:	2001062126 MEDLINE
DOCUMENT NUMBER:	20557651 PubMed ID: 11108264
TITLE:	The **melanin**-concentrating **hormone** receptor couples to multiple G proteins to activate diverse intracellular signaling pathways.
AUTHOR:	Hawes B E; Kil E; Green B; O'Neill K; Fried S; Graziano M P
CORPORATE SOURCE:	Central Nervous System/Cardiovascular Department, Schering-Plough Corp. Research Institute, Kenilworth, New Jersey 07033, USA.. brian.hawes@spcorp.com
SOURCE:	ENDOCRINOLOGY, (2000 Dec) 141 (12) 4524-32. Journal code: 0375040. ISSN: 0013-7227.
PUB. COUNTRY:	United States
DOCUMENT TYPE:	Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:	English
FILE SEGMENT:	Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH:	200012
ENTRY DATE:	Entered STN: 20010322 Last Updated on STN: 20021218 Entered Medline: 20001222

AB The receptor for **melanin**-concentrating **hormone** (MCH) was recently identified as the orphan G protein-coupled receptor **SLC**-1. In this study, a CHO cell line expressing the MCH receptor (Kd = 1.3 nM; **binding capacity**, 3.6 pmol/mg protein) is used to assess the ability of the MCH receptor to couple to Gi, Go, and Gq proteins. The results demonstrate that MCH inhibits forskolin-stimulated cAMP production in a pertussis toxin- (PTX)-sensitive

manner in CHO-MCHR cells (EC50 = 100 pM), indicating that the MCH receptor couples to one or more members of the Gi subfamily of G proteins. In addition, MCH stimulates increases in phosphoinositide metabolism (EC50 = 50 nM) and in intracellular free Ca2+ levels (EC50 = 10 nM). MCH-stimulated inositol phosphate production and increases in intracellular free Ca2+ are partially inhibited (60% and 40%, respectively) by PTX pretreatment, demonstrating that there are at least two components of each of these signaling pathways. One component is PTX sensitive and therefore mediated through a Gi/Go protein. A distinct G protein-coupled (probably Gq type) mediates the PTX-insensitive component. To distinguish Gi vs. Go coupling, MCH-stimulated mitogen-activated protein (MAP) kinase activity was examined. Gi and Go use separate signaling pathways to mediate MAP kinase activation in CHOcells. Protein kinase C (PKC) activity is essential in the Go-dependent MAP kinase signaling pathway, but is not required in the GC-dependent MAP kinase signaling pathway. MCH stimulated MAP kinase activity is decreased (50%), but not abolished, by inhibition of PKC activity or depletion of cellular PKC, indicating that MCH-stimulated MAP kinase activity is mediated through both Gi- and Go-dependent signaling mechanisms. The results of this study are the first to clearly demonstrate that the MCH receptor couples to multiple G proteins to mediate several diverse intracellular signaling pathways.

L34 ANSWER 25 OF 32 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:605562 HCAPLUS
DOCUMENT NUMBER: 133:247473
TITLE: Expression of melanin-concentrating hormone receptors in insulin-producing cells: MCH stimulates insulin release in RINm5F and CRI-G1 cell-lines
AUTHOR(S): Tadayyon, M.; Welters, H. J.; Haynes, A. C.; Cluderay, J. E.; Hervieu, G.
CORPORATE SOURCE: Department of Vascular Biology, SmithKline Beecham Pharmaceuticals, Harlow, CM19 5AD, UK
SOURCE: Biochemical and Biophysical Research Communications (2000), 275(2), 709-712
CODEN: BBRCA9; ISSN: 0006-291X
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Melanin-concg. hormone (MCH) is a hypothalamic orexigenic peptide. Recently, an orphan G-protein-coupled receptor (**SLC**-1) was identified that binds MCH with high affinity. The authors demonstrate mRNA expression of this receptor in insulin-producing cells including CRI-G1 and RINm5F cells, and in rat islets of Langerhans. Immunofluorescence studies in CRI-G1 and RINm5F cell-lines demonstrated cell-surface expression of the receptor. Rat MCH significantly stimulated insulin secretion in both cell-lines. The potency and the efficacy of MCH were significantly increased in the simultaneous presence of forskolin, suggesting that MCH may amplify the insulinotropic effect of cAMP elevating stimuli. Salmon MCH, which differs from rat/human MCH by six amino acids, was less efficacious than rat/human MCH in stimulating insulin release. The data provide evidence for the expression of MCH receptors in insulin producing cells. The insulinotropic effect of MCH may contribute to the regulation of metab. and energy balance by this peptide. (c) 2000 Academic Press.
REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 26 OF 32 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 2000:226141 BIOSIS
DOCUMENT NUMBER: PREV200000226141
TITLE: Isolation and identification of **melanin** -concentrating **hormone**(MCH) as the endogenous ligand of the **SLC**-1 receptor.
AUTHOR(S): **Shimomura, Yukio (1)**; **Sugo, Tsukasa (1)** ; **Ishibashi, Yoshihiro (1)**; Abe, Michiko (1); **Mori, Masaaki (1)**
CORPORATE SOURCE: (1) Discovery Research Laboratories I, Pharmaceutical Discovery Research Division, Takeda Chemical Industries, Ltd., Wadai 10, Tukuba, Ibaraki, 300-4293 Japan
SOURCE: Japanese Journal of Pharmacology, (2000) Vol. 82, No. Suppl. 1, pp. 128P.
Meeting Info.: 73rd Annual Meeting of the Japanese Pharmacological Society. Yokohama, Japan March 23-25, 2000
ISSN: 0021-5198.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

L34 ANSWER 27 OF 32 MEDLINE DUPLICATE 9
ACCESSION NUMBER: 1999373129 MEDLINE
DOCUMENT NUMBER: 99373129 PubMed ID: 10441476
TITLE: Isolation and identification of **melanin** -concentrating **hormone** as the endogenous ligand of the **SLC**-1 receptor.
AUTHOR: **Shimomura Y; Mori M; Sugo T; Ishibashi Y**; Abe M; Kurokawa T; Onda H; Nishimura O; Sumino Y; Fujino M
CORPORATE SOURCE: Pharmaceutical Discovery Research Division, Takeda Chemical Industries, Ltd., Wadai 10, Tsukuba, Ibaraki, 300-4293, Japan.
SOURCE: BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, (1999 Aug 11) 261 (3) 622-6.
Journal code: 0372516. ISSN: 0006-291X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199909
ENTRY DATE: Entered STN: 19990925
Last Updated on STN: 20000303
Entered Medline: 19990909

AB **Melanin**-concentrating **hormone** (MCH), which is an orexigenic peptide, was isolated and identified as the endogenous ligand of the **SLC**-1 receptor. We established a CHO cell line expressing the rat **SLC**-1 receptor to search for its endogenous ligand. The extract of rat whole brain showed inhibition of intracellular forskolin-induced cAMP accumulation in rat **SLC**-1-expressing CHO cells and was purified. Using HPLC purification, we isolated and identified MCH as the endogenous ligand of the **SLC**-1 receptor. The authentic MCH demonstrated a dose-dependent inhibitory effect on cAMP accumulation in forskolin-stimulated rat and human **SLC** -1-expressing CHO cells with an EC(50) value of 0.2 nM for both the rat and human **SLC**-1 receptors. This is the first description of the functional receptor for MCH.

L34 ANSWER 28 OF 32 MEDLINE

Search completed by David Schreiber 308-4292

ACCESSION NUMBER: 1999318000 MEDLINE
DOCUMENT NUMBER: 99318000 PubMed ID: 10391116
TITLE: Functional neurokinin NK-1 receptor expression in rat peritoneal mast cells.
AUTHOR: Okada T; Hirayama Y; Kishi S; Miyayasu K; Hiroi J; Fujii T
CORPORATE SOURCE: Department of Immunology and Inflammation, Medicinal Biology Research Laboratories, Fujisawa Pharmaceutical Co., Ltd., Osaka, Japan.
SOURCE: INFLAMMATION RESEARCH, (1999 May) 48 (5) 274-9. Journal code: 9508160. ISSN: 1023-3830.
PUB. COUNTRY: Switzerland
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199908
ENTRY DATE: Entered STN: 19990910
Last Updated on STN: 19990910
Entered Medline: 19990826

AB OBJECTIVE AND DESIGN: Recently, Ogawa et al. [17] reported that the peritoneal mast cells (PMCs) of rats can release histamine by substance P (SP) in a receptor-dependent manner. In the present study, we confirmed and extended their findings. MATERIAL: PMCs were isolated from six strains of rats. In some experiments, peritoneal cells in the non-MC fraction were used. METHODS: PMCs were incubated with SP, neurokinin (NK) receptor agonists or antagonists, and histamine content in the supernatant was measured. In the binding assay, PMCs were incubated with [125I]BH-SP together with SP or NK receptor antagonists. NK-1 receptor mRNA was detected using a reverse transcription-polymerase chain reaction (RT-PCR) assay. RESULTS: PMCs from **Slc**: Wistar and F344/NSlc were highly sensitive to SP, leading to histamine release, whereas those from **Slc**:SD and three other strains were not. PMCs from **Slc** :Wistar and F344/NSlc also released histamine in the presence of an NK-1 agonist. The histamine release induced by SP and the NK-1 agonist was inhibited by the NK-1 receptor antagonists, FK888 and CP-99,994. [125I]BH-SP binding experiments revealed that PMCs from **Slc** :Wistar rats possessed a single high affinity binding site for SP and that the binding was blocked by NK-1 receptor antagonists. Peritoneal cells in the non-MC fraction exhibited no appreciable binding. In the RT-PCR assay, expression of NK-1 receptor mRNA was evident in **Slc** :Wistar PMCs, but not in the non-MC fraction from **Slc**:Wistar or **Slc**: SD PMCs. CONCLUSION: These data demonstrate the existence of functional NK-1 receptors on freshly isolated PMCs in at least some strains of rats.

L34 ANSWER 29 OF 32 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1999:594293 HCAPLUS
DOCUMENT NUMBER: 131:295734
TITLE: The receptor for the orexigenic peptide melanin-concentrating hormone is a G-protein-coupled receptor
AUTHOR(S): Lembo, Paola M. C.; Grazzini, Eric; Cao, Jack; Hubatsch, Douglas A.; Pelletier, Manon; Hoffert, Cyrla; St-Onge, Stephane; Pou, Chantevy; Labrecque, Jean; Groblewski, Thierry; O'Donnell, Dajan; Payza, Kemal; Ahmad, Sultan; Walker, Philippe
CORPORATE SOURCE: AstraZeneca R and D Montreal, Quebec, QC, H4S 1Z9, Can.
SOURCE: Nature Cell Biology (1999), 1(5), 267-271 CODEN: NCBIFN; ISSN: 1465-7392

Search completed by David Schreiber 308-4292

PUBLISHER: Macmillan Magazines Ltd
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Gene-knockout studies of melanin-concg. hormone (MCH) and its effect on feeding and energy balance have firmly established MCH as an orexigenic (appetite-stimulating) peptide hormone. Here the authors identify MCH as the ligand for the orphan receptor **SLC**-1. The rat **SLC**-1 is activated by nanomolar concns. of MCH and is coupled to the G protein G.alpha.i/o. The pattern of **SLC**-1 mRNA expression coincides with the distribution of MCH-contg. nerve terminals and is consistent with the known central effects of MCH. The authors' identification of an MCH receptor could have implications for the development of new anti-obesity therapies.
REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 30 OF 32 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1999:491711 HCAPLUS
DOCUMENT NUMBER: 131:223941
TITLE: Molecular characterization of the melanin-concentrating-hormone receptor
AUTHOR(S): Saito, Yumiko; Nothacker, Hans-Peter; Wang, Zhiwei; Lin, Steven H. S.; Leslie, Frances; Civelli, Olivier
CORPORATE SOURCE: Department of Pharmacology, University of California, Irvine, Irvine, CA, 92697-4625, USA
SOURCE: Nature (London) (1999), 400(6741), 265-269
CODEN: NATUAS; ISSN: 0028-0836
PUBLISHER: Macmillan Magazines
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Orphan G-protein-coupled receptors (GPCRs) are cloned proteins with structural characteristics common to the GPCRs but that bind unidentified ligands. Orphan GPCRs have been used as targets to identify novel transmitter mols. Here we describe the isolation from brain exts. and the characterization of the natural ligand of a particular orphan GPCR (**SLC**-1) that is sequentially homologous to the somatostatin receptors. We show that the natural ligand of this receptor is the neuropeptide melanin-concg. hormone (MCH). MCH is a cyclic peptide that regulates a variety of functions in the mammalian brain, in particular feeding behavior. We demonstrate that nanomolar concns. of MCH strongly activate **SLC**-1-related pathways through G.alpha.i and/or G.alpha.q proteins. We have analyzed the tissue localization of the MCH receptor and find that it is expressed in several brain regions, in particular those involved in olfactory learning and reinforcement mechanisms, indicating that therapies targeting the MCH receptor should act on the neuronal regulation of food consumption.
REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 31 OF 32 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1999:491705 HCAPLUS
DOCUMENT NUMBER: 131:223721
TITLE: Melanin-concentrating hormone is the cognate ligand for the orphan G-protein-coupled receptor **SLC**-1
AUTHOR(S): Chambers, Jon; Ames, Robert S.; Bergsma, Derk; Muir, Alison; Fitzgerald, Laura R.; Hervieu, Guillaume; Dytko, George M.; Foley, James J.; Martins, John; Liu, Wu-Schyong; Park, Janet; Ellis, Catherine; Ganguly,

Subinay; Konchar, Susan; Cluderay, Jane; Leslie, Ron; Wilson, Shelagh; Sarau, Henry M.
CORPORATE SOURCE: Departments of Molecular Screening Technologies and Neuroscience, New Frontiers Science Park, SmithKline Beecham Pharmaceuticals, Essex, CM19 5AW, UK
SOURCE: Nature (London) (1999), 400(6741), 261-265
CODEN: NATUAS; ISSN: 0028-0836
PUBLISHER: Macmillan Magazines
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The underlying causes of obesity are poorly understood but probably involve complex interactions between many neurotransmitter and neuropeptide systems involved in the regulation of food intake and energy balance. Three pieces of evidence indicate that the neuropeptide melanin-concg. hormone (MCH) is an important component of this system. First, MCH stimulates feeding when injected directly into rat brains; second, the mRNA for the MCH precursor is upregulated in the hypothalamus of genetically obese mice and in fasted animals; and third, mice lacking MCH eat less and are lean. MCH antagonists might, therefore, provide a treatment for obesity. However, the development of such mols. has been hampered because the identity of the MCH receptor has been unknown until now. Here we show that the 353-amino-acid human orphan G-protein-coupled receptor **SLC**-1 (ref. 4) expressed in HEK293 cells binds MCH with sub-nanomolar affinity, and is stimulated by MCH to mobilize intracellular Ca2+ and reduce forskolin-elevated cAMP levels. We also show that **SLC**-1 mRNA and protein is expressed in the ventromedial and dorsomedial nuclei of the hypothalamus, consistent with a role for **SLC**-1 in mediating the effects of MCH on feeding.

L34 ANSWER 32 OF 32 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1996:639629 HCAPLUS
DOCUMENT NUMBER: 125:317650
TITLE: A new radioligand of human/rat **melanin** concentrating **hormone** (MCH) for receptor identification
AUTHOR(S): Drozdz, R.; Baker, B. I.; Eberle, A. N.
CORPORATE SOURCE: Department Research (ZLF), University Hospital, Basel, CH-4031, Switz.
SOURCE: Peptides 1994, Proceedings of the European Peptide Symposium, 23rd, Braga, Port., Sept. 4-10, 1994 (1995) , Meeting Date 1994, 785-786. Editor(s): Maia, Hernani L. S. ESCOM: Leiden, Neth.
CODEN: 63MBAO
DOCUMENT TYPE: Conference
LANGUAGE: English
AB The introduction of a tyrosine residue at the C-terminus of MCH proved to be very favorable for the prepn. of a potent and biol. active MCH radioligand, in contrast to previous attempts in which a residue suitable for radioiodination (tyrosine, **Bolton-Hunter** reagent) was introduced at the N-terminus of the MCH mol. Also, the replacement of Tyr 13 by phenylalanine did not affect the biol. activity of MCH. This demonstrates that the p-hydroxyl group of the Ph ring of Tyr 13 is not absolutely required for receptor binding.

Jiang 09/869,540

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L4               STR
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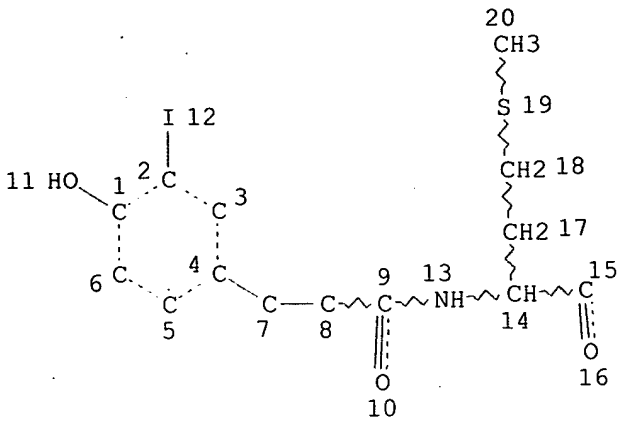


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NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
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NUMBER OF NODES IS  20

STEREO ATTRIBUTES: NONE
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L7             2 SEA FILE=HCAPLUS L6
L8             0 SEA FILE=HCAPLUS L7 AND L1


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DICTIONARY FILE UPDATES:  24 JUN 2003  HIGHEST RN 536971-45-6

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Crossover limits have been increased.  See HELP CROSSOVER for details.

Experimental and calculated property data are now available.  See HELP
PROPERTIES for more information.  See STNote 27, Searching Properties
in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

                Search completed by David Schreiber   308-4292
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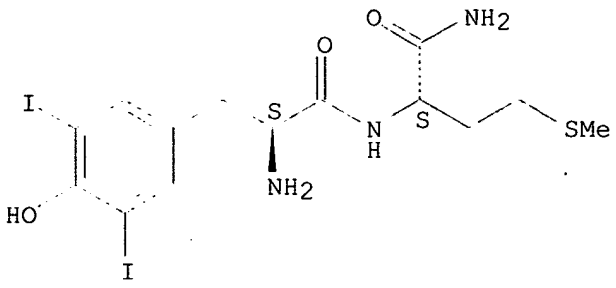
Jiang 09/869,540

=> d scan l6

L6 4 ANSWERS REGISTRY COPYRIGHT 2003 ACS
IN L-Methioninamide, 3,5-diiodo-L-tyrosyl- (9CI)
MF C14 H19 I2 N3 O3 S

Absolute stereochemistry.

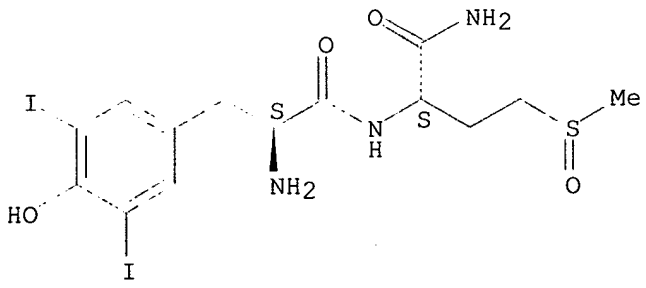


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):.

L6 4 ANSWERS REGISTRY COPYRIGHT 2003 ACS
IN Benzenepropanamide, .alpha.-amino-N-[(1S)-1-(aminocarbonyl)-3-(methylsulfinyl)propyl]-4-hydroxy-3,5-diiodo-, (.alpha.S)- (9CI)
MF C14 H19 I2 N3 O4 S

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

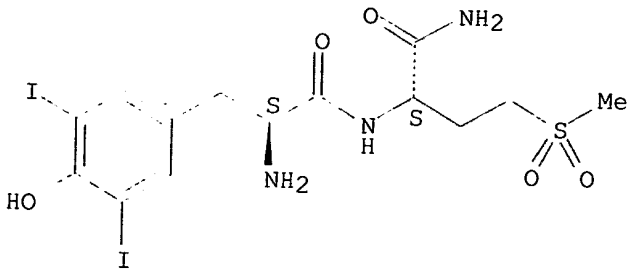
HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):.

L6 4 ANSWERS REGISTRY COPYRIGHT 2003 ACS
IN Benzenepropanamide, .alpha.-amino-N-[(1S)-1-(aminocarbonyl)-3-(methylsulfonyl)propyl]-4-hydroxy-3,5-diiodo-, (.alpha.S)- (9CI)
MF C14 H19 I2 N3 O5 S

Search completed by David Schreiber 308-4292

Jiang 09/869,540

Absolute stereochemistry.



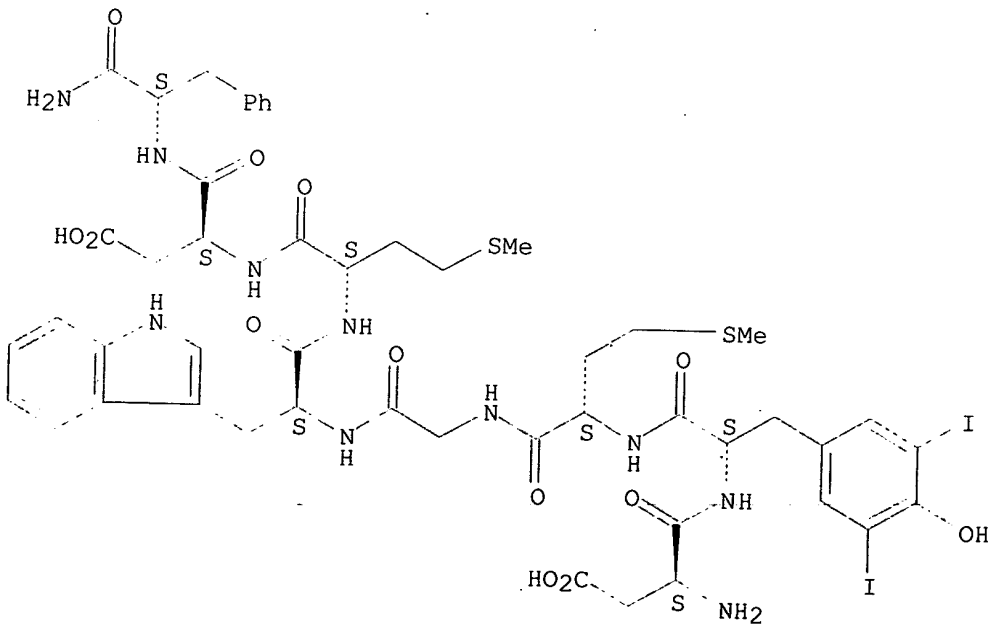
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):.

L6 4 ANSWERS REGISTRY COPYRIGHT 2003 ACS
IN Caerulein, 1-de(5-oxo-L-proline)-2-de-L-glutamine-4-(3,5-diiodo-L-tyrosine)-5-L-methionine- (9CI)
SQL 8
MF C49 H60 I2 N10 O13 S2

RELATED SEQUENCES AVAILABLE WITH SEQLINK

Absolute stereochemistry.



Search completed by David Schreiber 308-4292

Jiang 09/869,540

ALL ANSWERS HAVE BEEN SCANNED

Search completed by David Schreiber 308-4292